

SANS from P85/Water-*d* under Pressure

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Pluronics are triblock copolymers of poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide). Pluronic P85 forms a rich phase behavior when dissolved in water. Unimers are observed at low temperature while micelles form at higher temperatures. Spherical, cylindrical, and lamellar micelles are observed sequentially upon heating. The effect of hydrostatic pressure on the phase boundaries is investigated here using small-angle neutron scattering from a dilute P85 solution in deuterated water. The transition temperatures between these micelle phases are found to rise with increasing pressure. A new phase corresponding to demixed lamellae was observed at high temperature. The effect of pressure was seen to decrease the onset formation line of that new phase.

I. Introduction

Amphiphilic triblock copolymers composed of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO) in a PEO–PPO–PEO fashion have been the focus of much attention. Commercially known as Pluronics, this class of water-soluble copolymers has found a wide array of uses in industrial and medical applications. Pluronics have found industrial uses as detergents as well as foaming and emulsification agents.¹ Of particular interest is the biocompatibility of Pluronics, leading to many applications in the medical and pharmaceutical fields.^{2–5} Controlled drug release has proven to be a large use of Pluronics, as well as the solubilization of hydrophobic drugs within Pluronic micelles.

These numerous and wide-reaching uses stem from the amphiphilic nature of Pluronic copolymers. The PEO block is hydrophilic in nature and dissolves in water at all temperatures. This has been attributed to the oxygen–oxygen interdistance within the PEO chain, which is similar to the oxygen–oxygen interdistance in water.⁶ The PPO block, on the other hand, is hydrophobic and self-associates upon heating.

The behavior of Pluronics in aqueous solutions has been shown to depend on block architecture as well as temperature and pressure.^{7,8} The dependence on these thermodynamic properties is our main focus here. When these parameters are varied, Pluronics self-associate into a multitude of structures such as spherical, cylindrical, and lamellar micelles, as well as micellar

crystals. Few studies, however, have examined the pressure effects on the phase behavior of Pluronics in aqueous solution, as most have examined either architecture or temperature effects.

A review of the effect of pressure on phases in lipid and surfactant solutions has been presented by Winter.⁹ Most of the current literature examines the phase transitions between multiple lamellar or gel phases. Few studies have examined transitions between micelle-forming microstructures. A high pressure small-angle neutron scattering (SANS) study on an amphiphilic surfactant (pentaethylene glycol monooctyl ether, CH₃(CH₂)₇(OCH₂CH₂)₅OH) showed that the radius of gyration of spherical micelles in solution decreases between ambient pressure and 150 MPa.¹⁰ It was also shown that the hydrophobic core radius increases slightly with pressure, while the hydrophilic shell becomes dehydrated and its radius decreases. In a nuclear magnetic resonance (¹H NMR) study on the same surfactant, the critical micelle concentration (cmc) was examined as a function of pressure.¹¹ Up to a pressure of 150 MPa, the cmc was shown to decrease with increasing pressure, while above this pressure cmc values were shown to increase. In aqueous surfactant solutions, cmc and CMT (critical micelle temperature) values vary in opposite direction.

Recent literature searches found few pressure studies on the phase diagram of aqueous Pluronic solutions, with a limited number on nonionic aqueous surfactants.^{12,13} Both Kostko et al.¹² and Mortensen et al.¹⁴ examined concentrated (≥ 20 wt %) aqueous Pluronic solutions. Through dynamic light scattering studies, Kostko et al.¹² examined the Pluronic F108 (EO₁₄₁PO₄₄EO₁₄₁) and found that temperature boundaries between unimers, micelles, and clustered micelles increase with pressure. Mortensen et al.¹⁴

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examined Pluronic F88 ($\text{EO}_{96}\text{PO}_{39}\text{EO}_{96}$) by small-angle neutron scattering (SANS). It was observed that increasing pressure causes micelle decomposition and melting of micellar crystals. They observed that pressure enhances the solvent quality of water thereby shifting the cmc downward.

The temperature and volume fraction dependencies of Pluronic P85 ($\text{EO}_{26}\text{PO}_{40}\text{EO}_{26}$) have been studied extensively by Mortensen^{14,16} and Hammouda.¹⁷ SANS measurements done at ambient pressure have elucidated the volume fraction-temperature phase diagram for P85 in deuterated water (water-*d*). At low temperature and volume fraction, solvated unimers (dissolved copolymer chains) make up the solution. Neutron scattering from these unimers displays clustering at low-*Q* values, as well as chain solvation at high-*Q* (*Q* being the scattering variable). Clustering at low-*Q* has been observed in many water-soluble systems including polypeptide chains, polyelectrolyte solutions, as well as PEO in water-*d* solution. At relatively low volume fraction ($\phi < 10\%$), as temperature is increased, copolymers transition from unimers to spherical micelles at the cmc. These micelles then elongate into cylindrical (or rod-like) micelles, and finally lamellar micelles are formed.^{13,15–17} Higher order (micellar crystal) phases have also been observed at higher volume fractions.^{13,15,16}

In this study, we use SANS with in situ pressure to examine the pressure dependence of phase transitions in P85. This is important to understand the full phase diagram and develop greater uses for these copolymers.

II. Experimental Details

Materials. Pluronic P85 was obtained from BASF Corp., and was used as received. The average molecular weight of the copolymer is 4600 g/mol, as reported by the manufacturer. The copolymer has an average composition of $\text{EO}_{26}\text{PO}_{40}\text{EO}_{26}$.

Solution Preparation. Deuterium oxide, water-*d*, (99.9% D, from Cambridge Isotope Laboratories) was used as solvent in order to increase the scattering contrast and lower the incoherent scattering background in SANS experiments. All scattering experiments were performed on a 0.5% (w/w) P85/water-*d* solution. The sample fraction was kept low to avoid interparticle (either interchain or intermicelle) interaction effects. Such structure factor effects have been shown to appear at volume fractions as low as 4% (at approximately 43 °C).¹³

SANS. The SANS technique under high pressure was used to examine the phase transitions of the aqueous P85 solution. SANS measurements were made at the National Institute of Standards and Technology Center for Neutron Research (NCNR), on the NG3-SANS instrument. Sample-to-detector distances of 2 and 12 m were used with a 6 Å neutron wavelength.

The SANS in situ pressure cell uses two sapphire windows separated by a 1 mm gap in which the polymer solution is contained. The entire hydrostatic pressure pump and pressure cell were filled with the sample solution. Scattering measurements were taken at every 5 °C between 25 and 125 °C (± 0.3 °C), and at four different pressures: 2.76, 90, 179, and 269 MPa (corresponding to 400, 13000, 26000, and 39000 psi, respectively). The lowest pressure of 2.76 MPa was chosen to allow measurements at temperatures above the boiling point of water.

SANS Data Analysis. Polymer structures can be determined through distinct scattering patterns associated with form factors and fractal dimensions of scattering bodies. Examining both the high- and low-*Q* scattering behavior is necessary to obtain a full picture of the copolymer structures.

The $1/Q^m$ behavior, where *m* is the Porod exponent, is representative of the fractal dimension of a scattering body. Mass fractals are indicated by *m* values of 1 to 3, where 1 indicates high solvation and 3 indicates a collapsed molecule. Values of *m* between 3 and 4 represent surface fractals, where 3 indicates a rough surface and 4 a smooth surface. The various phases of a Pluronic in solution can be reliably determined through qualitative observations of these form factor and fractal dimension trends seen in SANS data.

A new empirical model that determines a Porod exponent as well as a radius of gyration (R_g) of a scattering body has been recently introduced.¹⁸ This so-called Guinier–Porod model simultaneously fits both the Guinier and Porod scattering regions of small-angle scattering curves. This single empirical model fits spherical, cylindrical, and lamellar structures as well as transition structures in-between.

In this model the following functional forms are used:

$$I(Q) = \frac{G}{Q^s} \exp\left(\frac{-Q^2 R_g^2}{3-s}\right), \quad \text{for } Q \leq Q_1 \quad (1)$$

and

$$I(Q) = \frac{D}{Q^m}, \quad \text{for } Q \geq Q_1 \quad (2)$$

The transition point between the Guinier and Porod scattering regions, Q_1 is obtained by imposing a smooth transition of the Guinier and Porod functions and their slopes. This yields:

$$Q_1 = \frac{1}{R_g} \sqrt{\frac{(m-s)(3-s)}{2}} \quad (3)$$

and the Porod scale factor *D* is given by:

$$D = \frac{G}{R_g(m-s)} \exp\left(\frac{(m-s)(3-s)}{2}\right)^{(m-s)/2} \quad (4)$$

Here, *G* is the Guinier scale factor and *m* is a Porod exponent. The term

$$\frac{G}{Q^s} \exp\left(\frac{-Q^2 R_g^2}{3-s}\right)$$

is referred to as the Guinier factor. The fitting parameter, *s*, determines the dimensionality of the scattering object. For spheres and other 3D objects, *s* = 0. Rods or cylinders have *s* = 1, and lamellae have *s* = 2.

III. Results and Discussion

SANS data were taken from 0.5% P85 in water-*d* as a function of both pressure and temperature, and both micelle formation and copolymer demixing were observed. At low temperatures, scattering from unimers in solution was observed. This displayed high intensity scattering at low-*Q*, known as clustering. At high-*Q*, a low intensity solvation signal was observed. The Porod exponent of the solvated unimer chains of $1/Q$ implies that unimers are stretched chains as they do not display the $1/Q^2$ behavior typical of Gaussian coils.

As temperature is increased, unimers self-associate to form spherical micelles, displaying the typical $1/Q^4$ behavior at high-*Q* and a flat low-*Q* signal. Upon further heating, the spherical micelles elongate into cylindrical micelles with $1/Q$ behavior at

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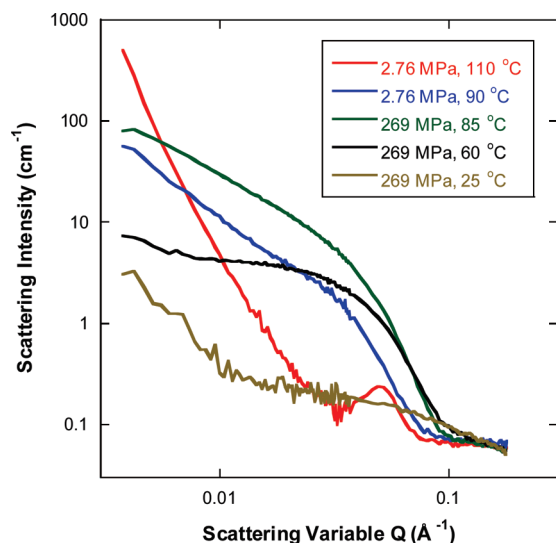


Figure 1. Scattering data from 0.5% P85/water-*d* solution at various pressure and temperature conditions. The 2.76 MPa and 110 °C data depicts a demixed lamellae structure, while the 2.76 MPa and 90 °C data represents lamellar micelles. Cylindrical micelles correspond to the 269 MPa and 85 °C data. The 269 MPa and 60 and 25 °C data correspond to spherical micelles and unimers in solution, respectively.

low- Q . Scattering typical of lamellae, $1/Q^2$ at low- Q , was seen at even higher temperatures (at 2.76 and 90 MPa for example). Each of these phases was previously observed at ambient pressure.

At temperatures above 95 °C, a Bragg peak forms at high- Q typical of interlamellar spacing. This phase is referred to as demixed lamellae. The lamellar micelles phase corresponds to uniformly distributed lamellae throughout the sample while in this new phase, lamellae are tightly stacked thereby forming pockets of solvent. The term “demixed lamellae” is preferred to “vesicles” since vesicles connote a spherical onionskin structure while it is not clear whether the newly observed structures are spherical. It should be noted that electron microscopy could not be performed at these high temperatures. The demixed lamellae phase is formed when the PEO outer blocks demix close to their cloud point temperature.¹⁹ Sample scattering data of each phase are displayed in Figure 1.

Interestingly, as temperature is held constant, it becomes clear that with increased pressure, the transition temperature between micellar phases increases. For example, at 65 °C, cylindrical micelles are present only at low pressures, while at high pressures, spherical micelles still exist (Figure 2). Note that at intermediated pressures, although the micelles are primarily spherical, both the scattering intensity and Porod exponents increase slightly. This indicates that the spheres are elongating and transitioning to cylindrical morphologies.

The various observed structures (unimers, spherical micelles, cylindrical micelles, lamellar micelles, and demixed lamellae) are shown schematically in Figure 3.

The specific transition temperatures between the copolymer micellar phases can be determined by monitoring the low- Q Guinier factor (eq 1) at a low- Q value of 0.004 Å⁻¹. In this way, phase transitions can be monitored. For example, the Guinier factor for unimers has a lower scattering intensity than that of spherical micelles, which, in turn, is less than that of cylindrical micelles.

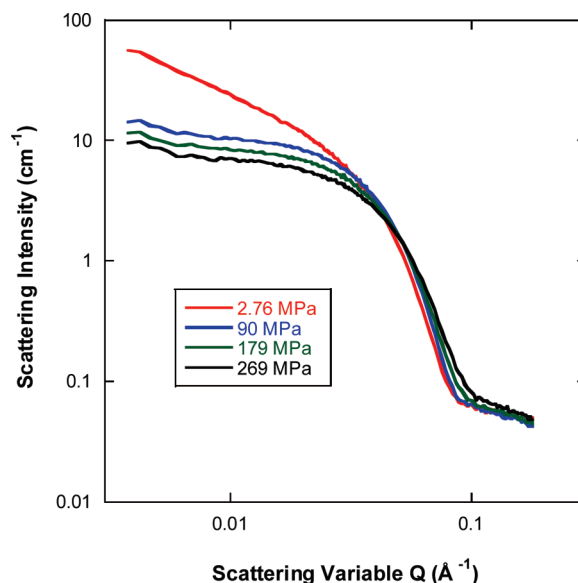


Figure 2. SANS scattering for 0.5% P85/water-*d* solution at fixed temperature of 65 °C and varying pressure. Cylindrical micelles are present at the lowest pressure, while spherical micelles remain in solution at high pressures.

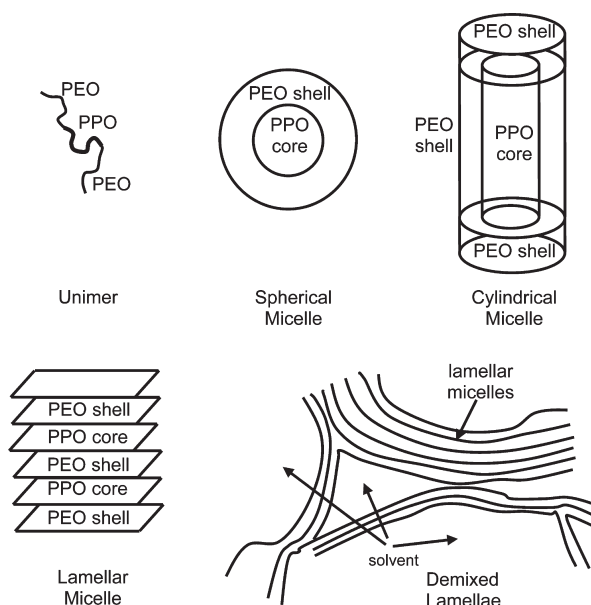


Figure 3. Schematic representation showing the observed structures.

Plotting this Guinier factor as a function of temperature, the transitions between copolymer morphologies are clear. The sigmoid shape of the Guinier factor between copolymer morphologies characterizes the transition temperatures between phases. This temperature is the midpoint between relative intensity plateaus. By determining these transition temperatures, the phase transition lines can be drawn for the system. The sigmoid shape of the Guinier factor is seen in Figure 4 for the measured pressures. Note that the empirical Guinier-Porod model is not appropriate to fit the (high temperature) demixed lamellae phase since a Bragg peak shows up.

Figure 5 shows the pressure effect on the phase transition lines. Transition temperatures between micelle morphologies were determined by the sigmoid method shown in Figure 4. The

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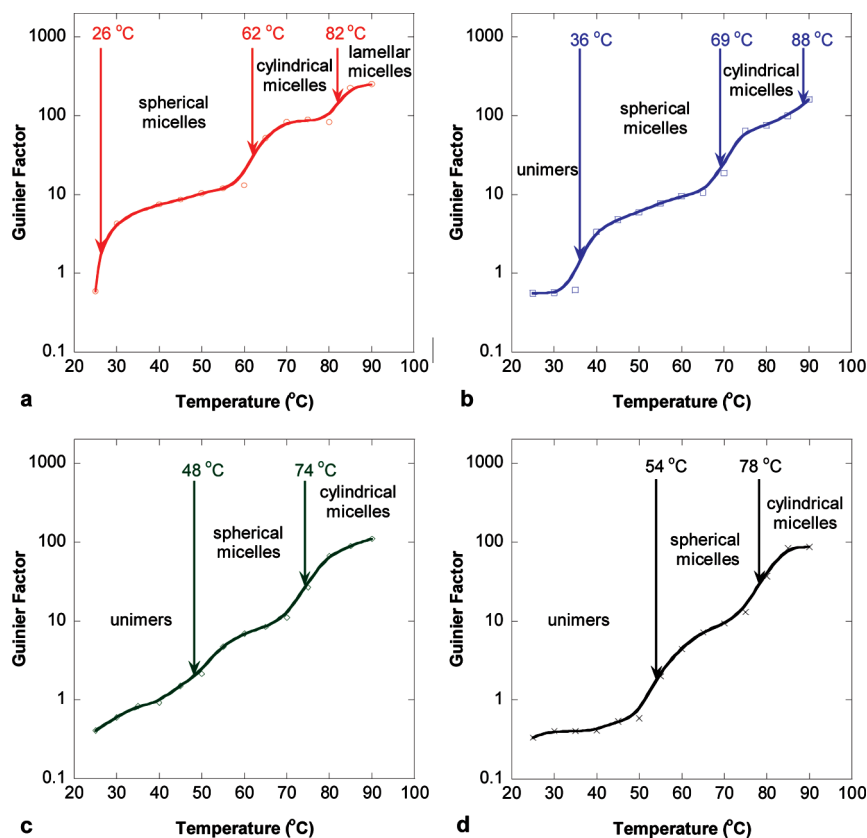


Figure 4. Variation of the Guinier factor with increasing temperature for 0.5% P85/water-*d* at the following pressures: (a) 2.76, (b) 90, (c) 179, and (d) 269 MPa. Transition temperatures between unimers, spherical micelles, cylindrical micelles, and lamellar micelles are indicated.

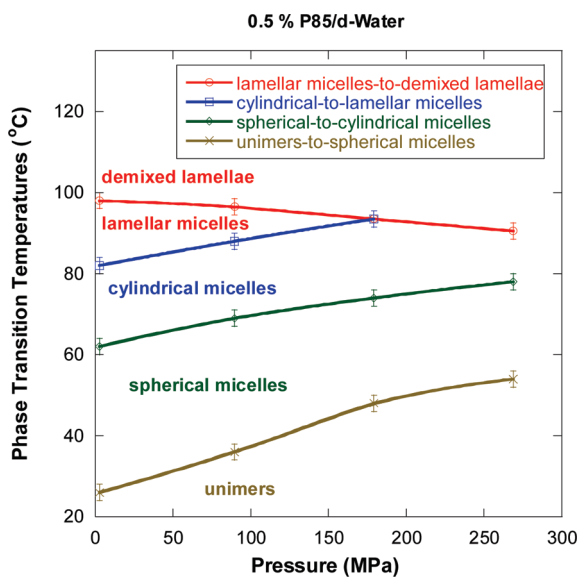


Figure 5. Effect of pressure on the phase boundary lines. Transitions between micelle morphologies were determined through the sigmoid variation of the Guinier factor, while the formation of the demixed micelle phase was determined by the appearance of the Bragg scattering peak. Statistical error bars correspond to one standard deviation.

demixed micelle transition was determined, instead, by the appearance of the Bragg peak in the scattering intensity data. Increased pressure is shown to shift micellar transition phase boundaries to higher temperatures. However, increasing pressure lowers the demixed lamella phase boundary as shown in Figure 5.

The pressure effect on phase boundary lines is substantial. For example, the unimers-to-spherical micelles transition increases by as much as 11 °C per kbar (note that 1 kbar = 101 MPa).

The increase of micellar phase transition boundaries with pressure can be thought of as a *copolymer* effect. Increasing pressure is equivalent to decreasing temperature. As discussed earlier, this is seen at 65 °C in the formation of cylindrical micelles at low pressures, while spherical micelles remain at high pressures (Figure 2). This leads to an increase of the transition temperature with pressure. This result is similar to the trends observed by Mortensen et al.¹⁴ who focused on narrower temperature (20 to 50 °C) and pressure (less than 1 kBar) windows.

The decrease of the demixed lamellae phase boundary with pressure can be understood as a *polymer solution* effect. This result is reminiscent of the effect of pressure on PEO/water solutions. PEO in water has been shown to phase separate upon heating, that is, it has a lower critical solution temperature (LCST). Hammouda et al.¹⁹ showed that pressure reduces the LCST of PEO/water solutions. It was argued that hydrogen bonds between the PEO polymer and solvent break at increased pressures, causing the polymer to demix from solution.

IV. Summary and Conclusions

The SANS characterization method has been used to investigate the various phase transitions in 0.5% P85 in water-*d*. Transitions from a unimer phase to a series of micellar phases (spherical, cylindrical, and lamellar) were observed. In situ hydrostatic pressure was found to increase the boundary lines between these micellar transitions. Another high-temperature phase referred to as the demixed lamellae phase was observed; its boundary line was found to decrease with increasing pressure.

The intermicelle transition lines are understood as a *copolymer* effect while the demixed lamellae phase is understood as a *polymer solution* effect.

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